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Amendments to the Specification

Please replace the paragraph beginning at page 14, line 15, with the following rewritten paragraph:

Figure 3A illustrates transmission spectrum for one (dotted line) and two (solid line) microspheres coupled to the same optical fiber, immersed in a PBS solution at room temperature. Both microspheres are ~200 μm in radius The narrow infrared spectrum ranging from 1312.92 to 1313 06 nm is recorded every 10 ms. The position of the resonance wavelengths from each of the microspheres S1 and S2 is located by a parabolic minimum fit in a resolution of ~1/50 of the linewidth, allowing detection of a fractional wavelength change $\delta\lambda/\lambda$ as small as ~$3x10^{-7}$. Both spheres were modified with unrelated, 27-mer oligonucleotides. Specifically, microsphere S1 was modified with 5'-biotin-TATGAATTCAATCCGTCGAGCAGAGTT (SEQ ID NO 1), and microsphere S2 was modified with 5'-biotin-ATTAATACGACTCACTATAGGGCGATG (SEQ ID NO 2).

Please replace the paragraph beginning at page 19, line 10, with the following rewritten paragraph:

At a given temperature, the salt concentration can be varied to determine this optimal salt concentration for the given temperature. Figure 4 illustrates the melting curves for match and mismatch hybridization of an 11-mer oligonucleotide (5'-biotin-CTATCTCAGTC) (SEQ ID NO 3) on a single microsphere as the salt concentration is varied.

Equilibrium resonance wavelength shifts were recorded after hybridization to the perfect match and to the 1 base pair (bp, a single nucleotide) mismatch sequence (3′-GATATAGTCAG) (SEQ ID NO 4) at different NaCl concentrations. It was determined that the hybridization signal from the matching sequence can be nearly ten times as large as the one from the mismatching sequence when the exemplary system is used in a 20 mM Tris buffer (pH 7.8) containing 30 mM NaCl at room temperature (~23°C).

Please replace the paragraph beginning at page 19, line 24, with the following rewritten paragraph:

The optimized temperature and salt concentration conditions determined experimentally were then used in a measurement with two microspheres. The first microsphere S1 was modified with the perfectly matching biotinylated 11-mer oligonucleotide sequence (5′-biotin-CTATCTCAGTC) (SEQ ID NO 3), while the second microsphere S2 carried the single nucleotide mismatch sequence (5′-biotin-CTATATCAGTC) (SEQ ID NO 5). Figure 5A shows a trace of the two resonances of the microspheres S1 and S2 over time. After temperature equilibration stabilized the traces, an 11-mer DNA strand was injected (to a final concentration of 1 μM) into the sample (See, arrow 510 at about 90 seconds) with a sequence which was complementary to the oligonucleotide immobilized on microsphere S1. As shown in Figure 5A, hybridization to the perfect match oligonucleotide on microsphere S1 produced a much larger increase in resonance wavelength than the hybridization to the oligonucleotide with the single nucleotide mismatch on microsphere S2. Specifically,

hybridization to the single mismatched sequence on microsphere S2 produced 1/10 of the increase, consistent with the hybridization data obtained in the single-sphere experiments using the same experimental conditions. Figure 5B is a plot of the difference signal which shows unambiguous identification of a single nucleotide mismatch with a high signal-to-noise ratio of 54 (where signal-to-noise ratio is calculated by dividing the wavelength shift of the difference signal after hybridization by the noise before hybridization). Note that the initial disturbances in the single traces (believed to be due to temperature and refractive index fluctuations in the surrounding media caused by turbulences after mixing with a hypodermic needle) are largely removed in the difference plot. Note that in Figure 5A, the graphed characteristic of microsphere S1 was moved up to separate it from that of microsphere S2 in order to simplify the drawing.